THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 17

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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Ex parte GRACE C. TSAY and NEAL CHEUNG

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Appeal No. 95-1231
Application No. 07/689,215[1]

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ON BRIEF

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Before WINTERS, HANLON and ROBINSON, Administrative Patent Judges.

ROBINSON, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 14 and 15, which are all of the claims pending in this application.

[1] Application for patent filed April 22, 1991.

An understanding of the invention can be derived from a reading of claims 14 and 15 which are reproduced below:

14. A method of determining the anticomplement activity of an immunoglobulin biological product intended for infusion, the method comprising the steps of

(A) contacting the product with human serum and then separately contacting the human serum with immobilized antibody preparations that specifically bind to complement component C1r and complement activation product C4a in the serum;

(B) separately measuring the amounts of the C1r and C4a that bind to the respective antibody preparations;

(C) comparing the amounts of the C1r and the C4a bound to the respective antibody preparations with standards to determine the amounts of C1r and C4a in the serum; and

(D) using the determinations of step (C) to determine the anticomplement activity of the product.

15. The method of claim 14 wherein the immunoglobulin product is an antibody preparation having a pH of about 4.25.

The references relied upon by the examiner are:

Bing, David H., "The Interaction of Immune Serum Globulin and Immune Globulin Intravenous with Complement." Molecule Immunology, vol. 20, No. 8, pp. 893-900 (1983).

Ziccardi et al. (Ziccardi), "Development of an Immunochemical Test to Assess C1 Inactivator Function in Human Serum and Its Use for the Diagnosis of Hereditary Angioedema." Clinical Immunology and Immunopathology, vol. 15, pp. 465-471 (1980).

Wagner et al., (Wagner), "Radioimmunoassay for Anaphylatoxins: A Sensitive Method for Determining Complement Activation Products in Biological Fluids." Analytical Biochemistry, vol. 136, pp. 75-88, (1984).

Grounds of Rejection

Claims 14-15 stand rejected under 35 U.S.C. § 112, first paragraph, as being based on a non-enabling disclosure.

Claims 14-15 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Bing, Wagner et al., and Ziccardi et al.

We reverse.

BACKGROUND

At page 4 of the specification, the applicants describe the invention as a method of determining the safety of a therapeutic immunoglobulin preparation comprising measuring its anticomplementary activity when mixed with human serum. The preferred embodiment is described as an assay wherein the immunoglobulin preparation is contacted with human serum and the human serum is then assayed for decreases in the specific complement component known as C1r and increases in the complement activation product known as C4a. Decreasing levels of C1r, combined with an increasing level of C4a are said to be indicative of the relative anticomplement activity and thus the safety of the immunoglobulin product being tested.

Discussion

The rejection under 35 U.S.C. § 112, first paragraph

Claims 14-15 stand rejected under 35 U.S.C. § 112, first paragraph, as being based on a non-enabling disclosure.

In the paragraph bridging page 3 and 4 of the Examiner's Answer (Answer), the examiner indicates the basis of the rejection:

> As recited, the claim requires contact of the product with human serum, and then separate contact of human serum with the immobilized antibody preparation . . . . the claim still does not clearly recite that the product is combined with human serum, and that two aliquots of this **combined** mixture are individually tested for binding to C1r and production of activation product C4a. Without such a combination, the assay cannot produce any meaningful result.

At page 7 of the Answer, the examiner concludes:

> Therefore, one of ordinary skill would have understood that "separately contacting the human serum with immobilized antibody preparation..." to mean the human serum control, and not human serum after contact with the product as alleged. In the absence of an explicit recitation of the contact of the product, human serum, and immobilized antibodies, the instant assay cannot function as intended.

It is axiomatic that, in proceedings before the PTO, claims in an application are to be given their broadest reasonable interpretation consistent with the specification and that claim language should be read in light of the specification as it would be interpreted by one of ordinary skill in the art. In re Sneed, 710 F.2d 1544, 1548, 218 USPQ 385, 388 (CAFC 1983). We do not agree that the examiner's interpretation of the claims is reasonable in light of the specification and as one of ordinary skill would read the noted

claim language. We find ourselves in agreement with appellants' statement at page 4 of the Appeal Brief (Brief) which states:

> In reading the claims, one skilled in the art would understand that after the contact of the test product with the human serum, C1r may be reduced and C4a may be generated within the serum. Hence, the serum then becomes the reagent used in the separate measurements of step (B).

We read the term "the" which precedes the phrase "human serum" in line 2 of step (A) to be indicative of an antecedent basis for the subject serum. We find no reference to the control human serum in the claim prior to this usage. The only use of the phrase "human serum" which precedes the use of the phrase in line 2 of Step (A) is that serum which has been contacted with the immunoglobulin product being tested. We conclude that the phrase "the human serum" refers to that serum previously contacted with the immunoglobulin product. We note that to accept the examiner's interpretation of the phrase as being directed not to the previously contacted human serum, but instead to human serum intended to act as the control, renders the claimed method of determining the anticomplement activity of the immunoglobulin product meaningless. Such a reading would result in data relating to the control serum and would not produce a determination of the anticomplement activity of the immunoglobulin product. We

choose not to give the claims such an unreasonable interpretation which is inconsistent with the invention as described in the specification.

The rejection under 35 U.S.C. § 112, first paragraph is reversed.

The rejection under 35 U.S.C. § 103

Claims 14 and 15 stand rejected under 35 U.S.C. § 103 as unpatentable over the combination of Bing, Wagner, and Ziccardi.

The claims before us are directed to a method of determining the anticomplement activity of an immunoglobulin product intended for infusion comprising contacting the immunoglobulin product with human serum and then contacting the human serum separately with immobilized antibody preparations to determine the amounts of complement component C1r and the complement activation product C4a in the serum. These determinations are then compared with standards to determine the anticomplement activity of the product.

The examiner's primary reference, Bing, is also concerned with determining the anticomplementary activity of immunoglobulin products through the determination of a complement component and a complement activation product following contacting the immunoglobulin product with a serum containing complement. However the reference differs from the claimed method in several ways. The examiner acknowledges at page 5 of the Answer that:

1) Bing measures for complement component C1q rather than C1r;

2) Bing measures for complement activation product C3a rather than C4a;

3) Bing uses competitive binding with ^{125}I-C1q rather than a direct binding assay for C1r; and

4) Bing uses crossed immunoelectrophoresis for determining the activation of C3a rather than a specific antibody binding to assay for C4a.

Wagner is relied upon by the examiner to establish the equivalence of the complement activation products C3a, C4a and C5a, all of which are released during the complement "classical pathway" activation. Wagner is said to also disclose the use of immunoassay for detection and quantifying of each of these products.

Ziccardi is relied upon by the examiner to establish as being old, an immunochemical test to assess the level of antigenically detectable C1r by radial immunodiffusion.

We have carefully considered the evidence and discussion in support of the rejection presented by the examiner. But on reflection and consideration of the claimed subject matter as a whole and the references relied upon, we find that the construction of the claimed method from the prior art teachings requires too much picking and choosing from the references cited to reach the claimed method in the absence of a clear suggestion to do so. While we agree that Bing is concerned with evaluating the safety of immunoglobulin products intended for administration to a patient, too many aspects of the Bing disclosure must be modified or a substitution made to reach the claimed method. To establish a prima facie case of obviousness, there must be more than the demonstrated

existence of all of the components. There must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill in the field of the invention would make the substitutions required. That knowledge can not come from the appellants' invention itself. Diversitech Corp. v. Century Steps, Inc., 850 F.2d 675, 678-79, 7 USPQ2d 1315, 1318 (Fed. Cir. 1988); In re Geiger, 815 F.2d 686, 688, 2 USPQ2d 1276, 1278 (Fed. Cir. 1987); Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1143, 227 USPQ 543, 551 (Fed. Cir. 1985). The extent to which such suggestion must be explicit in or may be fairly inferred from, the references, is decided on the facts of each case, in light of the prior art and its relationship to the invention. It is impermissible, however, simply to engage in a hindsight reconstruction of the claimed invention, using appellants' disclosure as a template and selecting elements from references to fill the gaps. In re Gorman, 933 F.2d 983, 986-987, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991). We find no reasonable suggestion for modifying Bing other than the disclosure provided by the applicants as to the specific aspects of the claimed method. The examiner has not established that it would have been obvious to one of ordinary skill in the art, at the time of the invention, to modify the method of Bing in such a manner as to arrive at the claimed method.

The rejection under 35 U.S.C. § 103 is reversed.

Summary

We reverse both the rejection of claims 14-15 under 35 U.S.C. § 112, first paragraph and the rejection of claims 14-15 under 35 U.S.C. § 103.

REVERSED

SHERMAN D. WINTERS Administrative Patent Judge	)	
ADRIENE LEPIANE HANLON Administrative Patent Judge	)	BOARD OF PATENT APPEALS AND INTERFERENCES
DOUGLAS W. ROBINSON Administrative Patent Judge	)	

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